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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

JUN 7 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: Coal Tar Creosote. Review of Acute Toxicity Studies, Guidelines 81-1 to 81-6.
Tox Chem No. 225
PC Code: 025004
Submission No. S455838
MRID Nos. 430321-01 to 430321-06 and 430323-01 to 430323-06
Case No. 818679
Action No. 625 6(a)(2)
DP Barcode No. D197959

From: Alberto Protzel, Ph.D. 5/26/94
Review Section III
Toxicology Branch II
Health Effects Division (7509C)

To: Mr.Eric Feris/Mr. Walter Waldrop (PM-71)
Reregistration Branch
Special Review and Registration Division (7508W)

Thru: James N. Rowe, Ph.D., Head James N. Rowe 5/26/94
Review Section III
Toxicology Branch II
Health Effects Division (7509C)

and

Marcia van Gemert, Ph.D., Chief m van Gemert 5/26/94
Toxicology Branch II
Health Effects Division (7509C)

ACTION:

TB-II has been asked to:

1. Review a series of mammalian acute toxicity studies (Guidelines 81-1 through 81-6) submitted by the Creosote Council II and Trenton Sales, Inc. of Houston TX in support of the Reregistration of Pesticide Products containing Coal Tar Creosote as the active ingredient and to make a determination as to their acceptability in satisfying guideline requirements .

2. Comment on the 6(a)(2) adverse effects status and how (or if) it should have an effect on the regulation of these compounds.

CONCLUSIONS :

1. Review of the mammalian acute toxicity studies and determination of their acceptability in satisfying guideline requirements.

All of the subject acute toxicity studies meet their respective guideline requirements, except for the following three studies with a classification of Supplementary:

a. Primary Dermal Irritation Test in Rabbits with North American P2 Creosote CTM. [Guideline 81-5; Study No. 671-010; MRID No. 430323-05]. This study may be upgraded to minimum.

b. Dermal Sensitization Study (Buehler) in the Albino Guinea pig with North American P2 Creosote CTM. [Guideline 81-6; Study No. 671-012; MRID No. 430323-06]. This study cannot be upgraded and must be repeated.

c. Dermal Sensitization Study (Buehler) in the Albino Guinea pig with North American P1/P13 Creosote CTM. [Guideline 81-6; Study No. 671-001; MRID No. 430321-01]. This study cannot be upgraded and must be repeated.

2. Comments on the 6(a)(2) status.

The data in the subject Acute Toxicity studies summarized below, do not indicate "unreasonable adverse effects on the environment" as stated in FIFRA 6(a)(2) and thus, the subject toxicity studies do not qualify as 6(a)(2) submissions.

DETAILED CONSIDERATIONS :

I. Background:

The Creosote Council II and Trenton Sales, Inc. of Houston TX have submitted a series of mammalian acute toxicity studies (Guidelines 81-1 through 81-6) in support of the Reregistration of Pesticide Products containing Coal Tar Creosote as the active ingredient. One set of acute toxicity studies was conducted with North American P1/P13 Creosote CTM [CAS No. 8001-58-9] and another set was conducted with North American P2 Creosote CTM [CAS No. 65996-92-1]. Both test materials are standard blends produced by the sponsor from creosotes from various industry sources. These materials are complex, multicomponent mixtures derived from coal tar.

II. Acute Toxicity of North American P1/P13 Creosote CTM [CAS No. 8001-58-9] and North American P2 Creosote CTM [CAS No. 65996-92-1].

As summarized in Table 1, below, toxicity categories for the subject chemicals are:

North American P1/P13 Creosote CTM:

- Category IV for acute inhalation (81-3).
- Category III for acute oral and dermal toxicity (81-1 & 81-2) and skin irritation (81-5).
- Category II for eye irritation (81-4).

North American P2 Creosote CTM:

- Category IV for acute inhalation (81-3)
- Category III for acute dermal toxicity (81-2), eye irritation (81-4), and oral toxicity (81-1).

No category is assigned to the acute skin irritation study conducted with North American P2 Creosote CTM (MRID 430323-05), pending submission of additional information, detailed below.

Table 1. Results of acute toxicity testing with North American P1/P13 and P2 Creosote CTMs.

Guideline	Test Type	Species	MRID	LD_{50} (mg/kg)	LC_{50} (4h) mg/l	Remarks	Toxicity Category	CORE Classification
				P1/P13 Creosote CTM				
81-1	Acute Oral	Rat	430321-01	2451 (♂), 1893 (♀)	-	Prostration & coldness to touch.	III	Minimum
81-2	Acute Dermal	Rabbit	430321-02	> 2000 (♂ & ♀)	-	No deaths or abnormal clinical signs.	III	Minimum
81-3	Acute Inhalation	Rat	430321-03	-	> 5	No mortality.	IV	Minimum
81-4	Eye Irritation	Rabbit	430321-04	-	-	Irritation clearing in 8-21 days.	II	Minimum
81-5	Skin Irritation	Rabbit	430321-05	-	-	Erythema (score = 2) on day 14.	III	Minimum
81-6	Dermal Sensitization	Guinea pig	430321-06	-	-	Results equivocal; study must be repeated.	-	Supplementary
				P2 Creosote CTM				
81-1	Acute Oral	Rat	430323-01	2524 (♂), 1993 (♀)	-	Prostration at doses $\geq$ 2000 mg/kg	III	Minimum
81-2	Acute Dermal	Rabbit	430323-02	>2000 (♂ & ♀)	-	No deaths or abnormal clinical signs.	III	Minimum
81-3	Acute Inhalation	Rat	430323-03	-	>5.3	Decreased activity at 5.3 mg/l	IV	Minimum
81-4	Eye Irritation	Rabbit	430323-04	-	-	Irritation clearing within 7 d. or less.	III	Minimum
81-5	Skin Irritation	Rabbit	430323-05	-	-	Study may be upgraded to Minimum	-	Supplementary
81-6	Dermal Sensitization	Guinea Pig	430323-06	-	-	Results equivocal; study must be repeated.	-	Supplementary

III. **Acceptability of the submitted studies in satisfying guideline requirements**.

As summarized in Table 1, all of the submitted acute toxicity studies with a CORE classification of Minimum meet their respective guideline requirement.

The following 3 studies with a classification of Supplementary do not meet their respective guideline requirement (reasons for the classification are included below with the DER summaries):

a. Primary Dermal Irritation Test in Rabbits with North American P2 Creosote CTM. [Guideline 81-5; Study No. 671-010; MRID No. 430323-05]. This study may be upgraded to minimum.

b. Dermal Sensitization Study (Buehler) in the Albino Guinea pig with North American P2 Creosote CTM. [Guideline 81-6; Study No. 671-012; MRID No. 430323-06]. This study is not upgradeable and must be repeated.

c. Dermal Sensitization Study (Buehler) in the Albino Guinea pig with North American P1/P13 Creosote CTM. [Guideline 81-6; Study No. 671-001; MRID No. 430321-01]. This study is not upgradeable and must be repeated.

IV. **Summaries of DERs for the submitted Acute Toxicity studies with North American P1/P13 Creosote CTM [CAS No. 8001-58-9] and North American P2 Creosote CTM [CAS No. 65996-92-1]**.

a. North American P1/P13 Creosote CTM [CAS No. 8001-58-9]

1. Acute Oral Toxicity in Rats (Guideline §81-1) -[Study 671-001; MRID 430321-1]

Crl:CD^{R} BR VAF/Plus^{R} rats (5 rats/sex/dose) from Charles River Laboratories, Inc., Portage, MI were administered orally North American P1/P13 Creosote CTM suspended in corn oil at doses of 1500, 2000, 2500, 3000, or 4000 mg/kg b.w. The acute oral LD_{50} values for males and females were 2451 and 1893 mg/kg, respectively. Pharmacotoxic signs observed during the 13 days following dosing included material around the mouth/nose, prostration and coldness to touch.

The study is classified as **Core Minimum Data (Acceptable)** with a **Toxicity Category III** and **satisfies** the requirement, § 81-1 for an acute oral toxicity study in rats (for North American P1/P13 Creosote CTM).

2. Acute Dermal Toxicity in Rabbits (Guideline §81-2 -[Study 671-003; MRID 430321-02].

New Zealand White (Hra:(NZW)SPF) rabbits (5 rabbits/sex/dose) from Hazleton Research Products, Inc., Kalamazoo, MI were administered undiluted North American Creosote Composite P1/P13, 2000 mg/kg b.w., to a shaved area in the back of approximately 15% of the body surface for 24 hours. No deaths or abnormal clinical signs were observed in any dose group. The acute dermal LD_{50} is greater than 2000 mg/kg for both sexes.

The study is classified as Core Minimum Data (Acceptable) with a Toxicity Category III and satisfies the requirement, § 81-2 for an acute dermal toxicity study in rabbits (for North American P1/P13 Creosote CTM).

3. Acute Inhalation Toxicity in Rats (Guideline §81-3 -[Study 671-005; MRID 430321-03].

Sprague-Dawley derived Crl:CD^R BR VAF/Plus^R rats (5 rats/sex/dose level) from Charles River Laboratories, Inc., Portage, MI; were exposed to North American P1/P13 Creosote CTM as an aerosol at nominal levels of 8.9 and 6.4 mg/l, corresponding to respective mean analytical levels of 5.0 (MMAD = 3.4 μm) and 0.6 (MMAD = 1.3 μm) mg/l, respectively, and then observed for 14 days. There was no mortality among treated rats. All low-dose and 9/10 high-dose rats exhibited decreased activity immediately after exposure. At the high dose, two of 5 males and 4/5 females exhibited decreased activity during the 14-day observation period. **The 4-hour inhalation LC_{50} for North American P1/P13 Creosote CTM is greater than 5 mg/l in rats.**

This study is classified as Core Minimum with **TOXICITY CATEGORY of IV for INHALATION (4-hr LC_{50} > 5 mg/l)**. This study satisfies the requirement, § 81-3 for an acute inhalation toxicity (LC_{50}) study in rats.

4. Primary Eye Irritation in Rabbits (Guideline 81-4) - [Study 671-007; MRID 430321-04].

New Zealand White (Hra:(NZW)SPF) rabbits (3 males and 3 females) from Hazleton Research Products, Inc., Kalamazoo, MI were administered 0.1 ml of undiluted North American Creosote Composite P1/P13 into the cupped conjunctival sac of the right eye. The cornea, iris and conjunctiva were scored (Draize) for eye irritation. There was no corneal or iridial irritation. Irritation of the conjunctiva in 3/6 animals) was seen in day 7 of observation but not on day 14.

The study is classified as Core Minimum Data (Acceptable) with a Toxicity Category II and satisfies the requirement, § 81-4 for a primary eye irritation study in rabbits (for North American P1/P13 Creosote CTM).

5. Primary Dermal Irritation in Rabbits (Guideline 81-5) - [Study 671-009; MRID 430321-05].

A 1 in^2 area of intact skin of New Zealand White (Hra:(NZW)SPF) rabbits (2 males and 4 females) from Hazleton Research Products, Inc., Kalamazoo, MI, was exposed to 0.5 ml of undiluted North American Creosote Composite P1/P13 for 4 hours. The primary skin irritation score indicated mild or slight irritation. However, one rabbit still had moderate edema (score = 3) on day 7 of observation and well defined erythema (score = 2) on day 14 of observation.

The study is classified as Core Minimum Data (Acceptable) with a Toxicity Category III and satisfies the requirement, § 81-5 for a primary skin irritation study in rabbits (for North American P1/P13 Creosote CTM).

6. Dermal Sensitization Study (Buehler) in the Albino Guinea Pig (Guideline 81-6) - [Study 671-011; MRID 430321-06].

Crl:(HA) BR (Albino Hartley) VAF/Plus Guinea pigs (10 animals/sex) from Charles River Laboratories, Inc., Portage, MI, were induced dermally with North American P1/P13 Creosote CTM (100% in corn oil) on study days 1, 7 and 14. Three weeks after the final induction, the test animals were challenged dermally with North American P1/P13 Creosote CTM (3% in corn oil). The challenge reaction was somewhat stronger, but not clearly different from that observed in previously untreated controls. Upon rechallenge 1 week later (with 3% test material in corn oil), the test animals gave a stronger reaction than that seen in the initial challenge. The untreated controls, however, had an unexpectedly strong irritation reaction that made the testing results equivocal. Positive controls (induced and challenged with 2,4-DNCB) gave a response that was unexpectedly weak. This equivocal test must be repeated based on the unexpectedly high reaction of the untreated controls and the weak positive control reaction.

The study is classified as Supplementary Data and does not satisfy the requirement, § 81-6 for a dermal sensitization study in Guinea pigs (for North American P1/P13 Creosote CTM).

b. North American P2 Creosote CTM [CAS No. 65996-92-1].

1. Acute Oral Toxicity in Rats (Guideline §81-1) -[Study 671-002; MRID 430323-1]

Crl:CD^{R} BR VAF/Plus^{R} rats (5 rats/sex/dose) from Charles River Laboratories, Inc., Portage, MI were administered orally North American P2 Creosote CTM suspended in corn oil at doses of 1000, 1500, 2000, 2300, 3000, or 3500 mg/kg/b.w. The acute oral LD_{50} values for males and females were 2524 and 1993 mg/kg, respectively. Pharmacotoxic signs observed during the 13 days following dosing included material around the mouth/nose and prostration.

The study is classified as Core Minimum Data (Acceptable) with a Toxicity Category III (LD_{50} from >500 through 5000 mg/kg) and satisfies the requirement, § 81-1 for an acute oral toxicity study in rats (for North American P2 Creosote CTM).

2. Acute Dermal Toxicity in Rabbits (Guideline §81-2) - [Study 671-004; MRID 430323-02].

New Zealand White (Hra:(NZW)SPF) rabbits (5 rabbits/sex/dose) from Hazleton Research Products, Inc., Kalamazoo, MI were administered undiluted North American Creosote Composite P2, 2000 mg/kg b.w., to a shaved area in the back of approximately 15% of the body surface for 24 hours. No deaths or abnormal clinical signs were observed in any dose group. The acute dermal LD_{50} is greater than 2000 mg/kg for both sexes.

The study is classified as Core Minimum Data (Acceptable) with a Toxicity Category III and satisfies the requirement, § 81-2 for an acute dermal

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toxicity study in rabbits (for North American P2 Creosote CTM).

3. Acute Inhalation Toxicity in Rats (Guideline §81-3 -[Study 671-006; MRID 430323-03].

Sprague-Dawley derived Crl:CD^{R} BR VAF/Plus^{R} rats (5 rats/sex/dose level) from Charles River Laboratories, Inc., Portage, MI; were exposed to North American P2 Creosote CTM as an aerosol at nominal levels of 10.9 and 9.9 mg/l, corresponding to respective mean analytical levels of 5.3 (MMAD = 2.9 μm) and 0.6 (MMAD = 1.3 μm) mg/l. There was no mortality among treated rats. All low-dose and high-dose rats exhibited decreased activity immediately after exposure. At the high dose, all males and 4/5 females exhibited decreased activity during the 14-day observation period. **The 4-hour inhalation LC_{50} for North American P2 Creosote CTM is greater than 5.3 mg/l in rats.**

This study is classified as Core Minimum with TOXICITY CATEGORY of IV for INHALATION (4-hr LC_{50} > 5 mg/l). This study **satisfies** the requirement, § 81-3 for an acute inhalation toxicity (LC_{50}) study in rats.

4. Primary Eye Irritation in Rabbits (Guideline 81-4) - [Study 671-008; MRID 430323-04].

New Zealand White (Hra:(NZW)SPF) rabbits (3 males and 3 females) from Hazleton Research Products, Inc., Kalamazoo, MI were administered 0.1 ml of undiluted North American Creosote Composite P2 into the cupped conjunctival sac of the right eye. The cornea, iris and conjunctiva were scored (Draize) for eye irritation. There was no corneal or iridial irritation. Irritation of the conjunctiva (in 3/6 animals) was seen at 96 hours of observation but not on day 7 of observation.

The study is classified as Core Minimum Data (Acceptable) with a Toxicity Category III and **satisfies** the requirement, § 81-4 for a primary eye irritation study in rabbits (for North American P2 Creosote CTM).

5. Primary Dermal Irritation in Rabbits (Guideline 81-5) - [Study 671-010; MRID 430323-05].

A 1-in^2 area of intact skin of New Zealand White rabbits (3 males and 3 females) from Hazleton Research Products, Inc., Kalamazoo, MI, was exposed to 0.5 ml of undiluted North American Creosote Composite P2 for 4 hours. At 72 hours, two rabbits had edema scores of 2, the others had scores of 0 or 1. No irritation (all scores were 0) was observed after 72 hours.

The study is classified as Core Supplementary Data with an assignment to a toxicity category deferred, pending submission of additional information. This study does not **satisfy** the requirement, § 81-5 for a primary skin irritation study in rabbits. This study may be **upgraded to Core Minimum** if the following additional information is provided and is judged to be acceptable:

1. Rationale for euthanization of two rabbits at 72 hours while the rest were

euthanized at 7 days.

2. A clarification concerning the "two groups" that were terminated due to technician error: Were these groups already treated with test material? Had they been scored for dermal irritation? If so, what were their irritation scores?

6. Dermal Sensitization Study (Buehler) in the Albino Guinea Pig (Guideline 81-6) - [Study 671-012; MRID 430323-06].

Crl:(HA) BR (Albino Hartley) VAF/Plus Guinea pigs (10 animals/sex) from Charles River Laboratories, Inc., Portage, MI, were induced dermally with North American P2 Creosote CTM (75% in corn oil) on study days 1, 7 and 14. Two weeks after the final induction, the test animals were challenged dermally with North American P2 Creosote CTM (3% in corn oil). The challenge reaction was more severe in the test animals than in controls, but the incidence was not clearly different in test animals (100%) than in controls (70%). The untreated controls had an unexpectedly high and variable reaction which made the evaluation of the results of this test equivocal. This equivocal test must be repeated based on the unexpectedly high and variable reaction of the untreated controls.

The study is classified as **Supplementary Data** and does not satisfy the requirement, § 81-6 for a dermal sensitization study in Guinea pigs (for North American P2 Creosote CTM).

Reviewed by: Alberto Protzel, Ph.D.
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D.
Section III, Tox. Branch II(7509C)

Alberto Protzel 3/29/94
James N. Rowe 3/29/94

DATA EVALUATION REPORT

STUDY TYPE: Acute oral toxicity in rats;
EPA Guideline 81-1

EPA IDENTIFICATION: EPA MRID No. 430321-01
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P1/P13 Creosote CTM

SYNONYMS: North American Creosote Composite P1/P13

STUDY NUMBER: 671-001

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Acute Oral Toxicity Study in Rats.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 9, 1993

EXECUTIVE SUMMARY: In an acute oral toxicity study, Crl:CD^{R} BR VAF/Plus^{R} rats (5 rats/sex/dose) from Charles River Laboratories, Inc., Portage, MI were administered orally North American P1/P13 Creosote CTM suspended in corn oil at doses of 1500, 2000, 2500, 3000, or 4000 mg/kg b.w. The acute oral LD_{50} values for males and females were 2451 and 1893 mg/kg, respectively. Pharmacotoxic signs observed during the 13 days following dosing included material around the mouth/nose, prostration and coldness to touch.

The study is classified as **Core Minimum Data** (Acceptable) with a **Toxicity Category III** and **satisfies** the requirement, § 81-1 for an acute oral toxicity study in rats (for North American P1/P13 Creosote CTM).

MATERIALS:

1. Test compound: North American P1/P13 Creosote CTM. Description: Black liquid; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424241-01. Additionally, Attachment 1 in the DER for MRID 430321-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P1/P13 in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. was stated as 8001-58-9.

2. Test animals: Species: rat, Strain: Charles River Crl:CD^{R} BR VAF/Plus^{R}; Age: 10 weeks old; Weight (at dosing): 279-350 g (males) and 179-230 g (females); Source: Charles River Laboratories, Inc., Portage, MI; Quarantine & acclimatization: 21 days.

METHODS:

Rats were fasted for about 18-20 hours before dosing. Test material was administered orally by gavage to 5 rats/sex/dose in corn oil in a volume of 20 ml/kg to give doses of 1500, 2000, 2500, 3000, or 4000 mg/kg/b.w. Animals were observed for mortality at 1, 2, and 4 hours after dosing on the first day and twice daily for 13 additional days. Pharmacotoxic signs were monitored at 1, 2, and 4 hours after dosing and once daily for 13 additional days. Rats were weighed prior to dosing, on day 8 and at study termination (day 15) or when the animal was found dead. All animals were necropsied for gross pathological examination.

The author noted that the test article was heated once to 80°C and again to approximately 40°C and stirred continuously using a motor driven propeller prior to being dispensed into an amber glass container. As noted in Attachment 2 in the DER for MRID 430321-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P1/P13 in Rats), the primary container with test material received from the sponsor (a 55-gallon drum) was heated to 80°C with a drum heater and stirred for 24 hours in order to obtain a homogeneous mixture. The test material was then transferred from the primary container to 33 secondary, 1-gallon containers for use in various tests. Prior to each test run, the secondary container was heated to 40°C and stirred.

RESULTS:

Pharmacotoxic signs during the first 4 hours after dosing included decreased activity at all dose levels (90-100%), low carriage (50-100%) at levels $\geq$ 2000 mg/kg. Decreased limb tone was seen in 1 rat at 3000 and 4000 mg/kg. Prostration was seen in 2 rats at 4000 mg/kg. Pharmacotoxic signs observed during the 13 days following dosing included material around the mouth/nose (50-80%) at all dose levels, prostration (50-70%) and was observed at levels $\geq$ 2500 mg/kg. Cold to touch was reported in 10% at $\leq$2000 and in 40-50% of the rats at higher doses. Mortality data are summarized in Table 1. The LD_{50} values for males and females were 2451 and 1893 mg/kg, respectively.

Gross necropsy revealed distended urinary bladder (frequency increasing with dose) at doses ≥ 2500. No effects on weight gain were observed.

Table 1. Mortality in rats after a single oral dose of North American P1/P13 Creosote CTM (From p. 11 of the Study Report).

Dose mg/kg	Males deaths/dosed	Females deaths/dosed
1500	0/5	1/5
2000	0/5	2/5
2500	4/5	5/5
3000	4/5	5/5
4000	5/5	5/5
LD_{50}(95%CL)[a] =	2451(2182-2753) mg/kg	1893(1628-2201) mg/kg

[a] The combined LD_{50}(95%CL) for males and females was 2197 (1927-2504) mg/kg.

Signed and dated quality assurance and GLP compliance statements were present.

Reviewed by: Alberto Protzel, Ph.D.
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D
Section III, Tox. Branch II(7509C)

Alberto Protzel 5/20/94
James N. Rowe 5/23/94

DATA EVALUATION REPORT

STUDY TYPE: Acute dermal toxicity in rabbits;
EPA Guideline 81-2

EPA IDENTIFICATION: EPA MRID No. 430321-02
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P1/P13 Creosote CTM

SYNONYMS: North American Creosote Composite P1/P13

STUDY NUMBER: 671-003

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Acute Dermal Toxicity Study in Rabbits.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 9, 1993

EXECUTIVE SUMMARY: In an acute dermal toxicity study, New Zealand White (Hra:(NZW)SPF) rabbits (5 rabbits/sex/dose) from Hazleton Research Products, Inc., Kalamazoo, MI were administered undiluted North American Creosote Composite P1/P13, 2000 mg/kg b.w., to a shaved area in the back of approximately 15% of the body surface for 24 hours. No deaths or abnormal clinical signs were observed in any dose group. The acute dermal LD_{50} is greater than 2000 mg/kg for both sexes.

The study is classified as **Core Minimum Data (Acceptable)** with a **Toxicity Category III** and **satisfies** the requirement, § 81-2 for an acute dermal toxicity study in rabbits (for North American P1/P13 Creosote CTM).

MATERIALS:

1. Test compound: North American P1/P13 Creosote CTM. Description: Black liquid; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424241-01. Additionally, Attachment 1 in the DER for MRID 430321-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P1/P13 in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. of the test material was stated to be 8001-58-9.

2. Test animals: Species: rabbit, Strain: New Zealand White (Hra:(NZW)SPF); Age: Approx. 3 1/2 months old; Weight (at dosing): 2380-2614 g (males) and 2275-2436 g (females); Source: Hazleton Research Products, Inc., Kalamazoo, Michigan. Quarantine: 10 days.

METHODS:

Groups of five male and five female rabbits had 2000 mg/kg of test material applied evenly (as received with no dilution) to a shaved area of the back. Hair was removed on the day prior to dosing with an electric clipper. The application area comprised approximately 15% of the body surface of the rabbit. The test area was covered with gauze and secured with Dermiform^{R} tape. Twenty four hours after treatment, the dressing was removed and the treated site was washed with water dried with disposable towels. The rabbits were observed for mortality 1, 2, and 4 hours after dosing on the first day, twice daily for 13 additional days, and once on the last day. The rabbits were observed for pharmacotoxic signs at 1, 2, and 4 hours after dosing on the first day, once daily for 13 additional days. Body weights were determined prior to dosing, on day 6 and at study termination (day 16).

The test article was heated once to 80°C and again to approximately 40°C and stirred continuously using a motor driven propeller prior to being dispensed into an amber glass container.

RESULTS:

No animals died during the study. No pharmacotoxic signs or body weight effects were seen and no abnormalities were observed at gross necropsy. The author concluded that the dermal LD_{50} was > 2000 mg/kg.

Signed and dated quality assurance and GLP compliance statements were present.

Reviewed by: Alberto Protzel, Ph.D.
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Secondary reviewer: James N. Rowe, Ph.D.
Section III, Tox. Branch II(7509C)

3/23/94
3/28/94

DATA EVALUATION REPORT

STUDY TYPE: Acute inhalation toxicity in rats;
EPA Guideline 81-3

EPA IDENTIFICATION : EPA MRID No. 430321-03
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P1/P13 Creosote CTM

SYNONYMS: North American Creosote Composite P1/P13

STUDY NUMBER: 671-005

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Acute Inhalation Toxicity Evaluation on North American Creosote Composite P1/P13 in Rats.

AUTHOR(S): Roger J. Hilaski

REPORT ISSUED: November 10, 1993

EXECUTIVE SUMMARY: In an acute inhalation toxicity study, Sprague-Dawley derived Crl:CD^{R} BR VAF/Plus^{R} rats (5 rats/sex/dose level) from Charles River Laboratories, Inc., Portage, MI; were exposed to North American P1/P13 Creosote CTM as an aerosol at nominal levels of 8.9 and 6.4 mg/l, corresponding to mean analytical levels of 5.0 (MMAD = 3.4 μm) and 0.6 (MMAD = 1.3 μm) mg/l, respectively, and then observed for 14 days. There was no mortality among treated rats. All low-dose and 9/10 high-dose rats exhibited decreased activity immediately after exposure. At the high dose, two of 5 males and 4/5 females exhibited decreased activity during the 14-day observation period. **The 4-hour inhalation LC_{50} for North American P1/P13 Creosote CTM is greater than 5 mg/l in rats.**

This study is classified as Core Minimum with TOXICITY CATEGORY of IV for INHALATION (4-hr LC_{50} > 5 mg/l). This study **satisfies** the requirement, § 81-3 for an acute inhalation toxicity (LC_{50}) study in rats.

MATERIALS:

1. Test compound: North American P1/P13 Creosote CTM. Description: Black liquid; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424241-01. Additionally, a list of the components in the test material having concentrations greater than 0.5% appears in Attachment 1 of this DER. The CAS No. of the test material was stated to be 8001-58-9.

2. Test animals: Species: rat; Strain: Sprague-Dawley derived Crl:CD^{R} BR VAF/Plus^{R}; Age: 53-75 days of age; Weight (at dosing): 234-283 g (males) and 192-216 g (females); Source: Charles River Laboratories, Inc., Portage, MI; Quarantine & acclimatization: at least 11 days.

METHODS:

Groups of five male and five female rats per dose were exposed (whole body exposure) for 4 hours to North American P1/P13 Creosote CTM as an aerosol, at nominal levels of 8.9 and 6.4 mg/l, corresponding to mean analytical levels of 5.0 (Group II) and 0.6 (Group III) mg/l.

A third group of animals ("Group I") was also exposed, but due to technical difficulties with the generation system, as noted by the author, the exposure was terminated. The data from this terminated experiment were not included in the Study Report. This reviewer notes that because group II (5.0 mg/l) consists of the Limit Dose and there were no deaths, data from the terminated experiment (Group I) are not required.

The animals were observed for mortality and toxic signs following exposure. The animals were observed for toxic signs (once daily) and for mortality (twice daily) during the 14-day post-exposure period. Body weights were recorded before exposure, and at 7 and 14 days post-exposure. All animals were subjected to gross pathological observation. No tissues were saved.

It was noted by the authors (Attachment 2 of this DER) that, initially, the primary container with test material received from the sponsor (a 55-gallon drum) was heated to 80°C with a drum heater and stirred for 24 hours in order to obtain a homogeneous mixture. The test material was then transferred from the primary container to 33 secondary, 1-gallon containers for use in various tests. Prior to each test run, the secondary container containing the test material aliquot used in the study was heated to 40°C and stirred.

To generate the exposure atmospheres, the test material was pumped to a Spraying Systems atomizer for formation of an aerosol that was discharged into a 4-liter glass atomization chamber. Purge-airflow swept the aerosol from the atomization chamber into the 160-liter stainless steel and glass exposure chamber. The exposure chamber was exhausted into a fume hood. Chamber airflow rates were 44 l/min (about 16.5 chamber volumes/hour at the high dose) and 106 l/min (about 39.7 chamber volumes/hour at the low dose). The exposure atmosphere was sampled (4 samples/dose; site and time of sampling were unspecified) at rates of 1-2 liters/minute for total volumes of 6-10 liters. Test material was collected in

tared glass fiber filters for determination of chamber concentrations. Aerosol particle size distribution was determined with an Andersen[R] 8-stage cascade impactor.

Although the author indicated that the animals were housed in individual steel wire cages it was not explicitly indicated that the animals were in individual cages during exposure.

RESULTS:

The analytical concentrations (in mg/l) were:
low dose: Mean of 0.6 and standard deviation of 0.06.
high dose: Mean of 5.0 and standard deviation of 0.10

The mass median aerodynamic diameter (MMAD) was:
- o 3.4 μm (geometric standard deviation of 1.89) at 5.0 mg/l, and
- o 1.3 μm (geometric standard deviation of 1.64) at 0.6 mg/l.

There were no deaths in this study and no significant macroscopic abnormalities were noted at necropsy. The following effects were observed:

- o Low dose (0.6 mg/l): All animals exhibited decreased activity immediately after exposure. Two males exhibited decreased activity during the 14-day observation period. Body weight gain was depressed for both sexes for weeks 1 and 2 after exposure.

- o High dose (5 mg/l): Immediately after exposure all animals were stained with the black test material, 9/10 exhibited decreased activity, and 3/5 males and 1/5 females exhibited increased salivation. Two of 5 males and 4/5 females exhibited decreased activity during the 14-day observation period. Body weight gain was depressed for females for weeks 1 and 2 after exposure.

The LC_{50} for North American Creosote Composite P1/P13 is greater than 5 mg/l for a 4-hour exposure.

Signed and dated quality assurance and GLP compliance statements were present.

Attachment 1
From page 41 of the Study Report .

Table 1. Creosote Target Analytes Greater than 0.5% by weight in P1 and P2 Composite Test Mixture Creosotes.

Target Analytes	P1 Composite (%)	P2 Composite (%)
Dihydroindene (Indan)	0.67 ± .004	0.67 ± .014
Indene	1.45 ± .010	1.22 ± .027
Naphthalene	10.86 ± .079	10.99 ± .249
Benzo(b)thiophene	0.48 ± .011	0.51 ± .009
Quinoline	1.30 ± .012	1.47 ± .044
2-Methylnaphthalene	5.37 ± .035	5.23 ± .189
1-Methylnaphthalene	2.68 ± .020	2.64 ± .070
Biphenyl	1.21 ± .011	1.31 ± .053
Acenaphthene	6.27 ± .045	7.00 ± .271
Dibenzofuran	4.80 ± .039	5.74 ± .222
Fluorene	4.27 ± .030	4.94 ± .188
Dibenzothiophene	1.44 ± .093	1.53 ± .121
Phenanthrene	12.66 ± .681	13.51 ± .901
Anthracene	1.33 ± .074	1.42 ± .097
Carbazole	1.23 ± 0.56	1.23 ± .076
4H-cyclopenta[*def*]phenanthrene	1.84 ± .038	1.80 ± .151
Fluorenthene	6.90 ± .299	6.92 ± .451
Pyrene	5.47 ± .234	5.34 ± .348
2,3-Benzofluorene	1.04 ± .033	1.01 ± .082
Benz[*a*]anthracene	1.02 ± .055	1.00 ± .082
Chrysene	0.99 ± .007	1.04 ± .079
Benzo(*b*)fluoranthene	0.58 ± .014	0.57± .054
Benzo(*k*)fluoranthene**	0.23 ± .006	0.23 ± .027
Total % (by weight)	74.09 ± 1.58	77.32 ± 3.30

**Benzo(k)fluoranthene was determined to be greater than the 0.5% by weight using GC/MS so it was included in this list.

As a Percent (%) of Creosote	Date Analyzed 8/26/92	8/31/92	Reported Composition (%)*
Naphthalene	8.97	8.85	10.86
2-Methylnaphthalene	5.48	4.58	5.37
1-Methylnaphthalene	2.01	1.94	2.68
Acenaphthene	5.22	5.16	6.27
Dibenzofuran	3.02	3.18	4.80
Fluorene	3.57	3.50	4.27
Phenanthrene	11.3	11.7	12.66
Fluoranthene	6.05	5.98	6.90
Pyrene	4.81	4.71	5.47

*Quantitative and Qualitative Determination of Creosote by Gas Chromatography/Flame Ionization (GCIFID), Geochemical and Environmental Reasearch Group (GERG), SOP-9206, July 23, 1992.

When development studies began, the primary container (55-gallon drum) was heated to 80°C with a drum heater and stirred for 24 hours in order to obtain a homogenous mixture. The test material was transferred from the primary container to 33 secondary containers (approximately one gallon each). Prior to all test runs and exposures, the secondary container was heated to 40°C and stirred. The test material and compound reservoir were examined for any undissolved/unsuspended solids, if a residue was observed the material was allowed to mix, while heating for additional time (2-2.5 hours) until completely redissolved/resuspended. The test material was heated and stirred throughout the test runs and exposures.

METHODS

EXPERIMENTAL DESIGN:

This study was designed to determine the acute inhalation toxicological effects in rats exposed, whole-body, to North American P1/P13 Creosote CTM. The experimental design was conducted such that the first exposure level was at a concentration of 5 mg/L or the maximum obtainable at any respirable aerosol size. Since no deaths occurred, the second exposure level was the maximum obtainable concentration where at least 25% of the aerosol was one micrometer (or less) in diameter.

Reviewed by: Alberto Protzel, Ph.D.
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D.
Section III, Tox. Branch II(7509C)

Alberto Protzel 5/26/94
James N. Rowe 5/26/94

DATA EVALUATION REPORT

STUDY TYPE: Primary Eye Irritation in rabbits;
EPA Guideline 81-4

EPA IDENTIFICATION : EPA MRID No. 430321-04
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P1/P13 Creosote CTM

SYNONYMS: North American Creosote Composite P1/P13

STUDY NUMBER: 671-007

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Eye Irritation Study in Rabbits.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 9, 1993

EXECUTIVE SUMMARY: In a primary eye irritation study, New Zealand White (Hra:(NZW)SPF) rabbits (3 males and 3 females) from Hazleton Research Products, Inc., Kalamazoo, MI were administered 0.1 ml of undiluted North American Creosote Composite P1/P13 into the cupped conjunctival sac of the right eye. The cornea, iris and conjunctiva were scored (Draize) for eye irritation. There was no corneal or iridial irritation. Irritation of the conjunctiva in 3/6 animals) was seen in day 7 of observation but not on day 14.

The study is classified as **Core Minimum Data (Acceptable)** with a **Toxicity Category II** and **satisfies** the requirement, § 81-4 for a primary eye irritation study in rabbits (for North American P1/P13 Creosote CTM).

MATERIALS:

1. Test compound: North American P1/P13 Creosote CTM. Description: Black liquid with pH of 5; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424241-01. Additionally, Attachment 1 in the DER for MRID 430321-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P1/P13 in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. of the test material was stated to be 8001-58-9.

2. Test animals: Species: rabbit, Strain: New Zealand White (Hra:(NZW)SPF); Age: Approx. 3 1/2 months old; Weight (at dosing): 2630-2794 g (males) and 2496-2579 g (females); Source: Hazleton Research Products, Inc., Kalamazoo, Michigan. Quarantine: 16 days.

METHODS:

One group of 3 male and 3 female rabbits was administered 0.1 ml of test material/rabbit into the cupped conjunctival sac of the right eye. The eyelids were gently held together for one second after administration. The eyes remained unwashed. The left eye was manipulated as the right eye, but received no test material and served as control. The rabbits were observed for the occurrence of vocalization. Both eyes were examined according to a Draize scale at 1, 24, 48, 72, and 96 hours and at 7 and 14 days after dosing. Sodium fluorescein examinations were conducted at 72 hours and at 7 and 14 days. The animals were observed for mortality once during the day of treatment and twice daily during the subsequent observation period. Individual data for each rabbit were presented.

The test article was heated once to 80°C and again to approximately 40°C and stirred continuously using a motor driven propeller prior to being dispensed into an amber glass container .

RESULTS:

No animals died and no overt signs of toxicity were observed during the study. No vocalization or signs of distress were observed. No effects were observed on the cornea or the iris of the six rabbits (all corneal and iris scores were 0). Fluorescein staining was negative. There was conjunctival redness (maximum scores of 2 or 3) in all animals for at least 48 hours. Three of six animals had conjunctival redness through day 7, achieving a score of 0 at day 14 of observation. Chemosis was observed in all rabbits for at least 24 hours. Two of six animals showed chemosis (score of 1: any swelling above normal) through day 7, achieving a score of 0 at day 14 of observation. Two of six animals had some degree of discharge, limited to the first hour after exposure. Average scores on day 7 and 14 were 1.7 and 0.0, respectively. The test material is classified as belonging in Toxicity Category II (irritation clearing in 8 to 21 days).

Signed and dated quality assurance and GLP compliance statements were present.

Reviewed by: Alberto Protzel, Ph.D. 5/24/94
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D. 5/24/94
Section III, Tox. Branch II(7509C)

DATA EVALUATION REPORT

STUDY TYPE: Primary Dermal Irritation in rabbits;
EPA Guideline 81-5

EPA IDENTIFICATION : EPA MRID No. 430321-05
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P1/P13 Creosote CTM

SYNONYMS: North American Creosote Composite P1/P13

STUDY NUMBER: 671-009

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Primary Dermal Irritation Test in Rabbits.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 9, 1993

EXECUTIVE SUMMARY: In a primary skin irritation study, a 1 in^2 area of intact skin of New Zealand White (Hra:(NZW)SPF) rabbits (2 males and 4 females) from Hazleton Research Products, Inc., Kalamazoo, MI, was exposed to 0.5 ml of undiluted North American Creosote Composite P1/P13 for 4 hours. The primary skin irritation score indicated mild or slight irritation. However, one rabbit still had moderate edema (score = 3) on day 7 of observation and well defined erythema (score = 2) on day 14 of observation.

The study is classified as **Core Minimum Data** (Acceptable) with a **Toxicity Category III** and satisfies the requirement, § 81-5 for a primary skin irritation study in rabbits (for North American P1/P13 Creosote CTM).

MATERIALS:

1. Test compound: North American P1/P13 Creosote CTM. Description: Black liquid with pH of 5; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424241-01. Additionally, Attachment 1 in the DER for MRID 430321-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P1/P13 in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. of the test material was stated to be 8001-58-9.

2. Test animals: Species: rabbit, Strain: New Zealand White (Hra:(NZW)SPF); Age: Approx. 3 1/2 months old; Weight (at dosing): 2566-2691 g (males) and 2440-2689 g (females); Source: Hazleton Research Products, Inc., Kalamazoo, Michigan. Acclimation: 9 days.

METHODS:

The dorsal hair of six rabbits (2 males, 4 females) was clipped using electric clippers. One application (intact skin) site on the back was delineated with indelible marker. A total of 0.5 ml of the test material was applied undiluted to the site. The site was covered with 1 in^2 gauze patch, secured with strips of non-irritating tape and then wrapped with 8-ply gauze bandaging and Dermiform® tape. Four hours after treatment, dressings were removed and the test area was washed thoroughly with water and dried with disposable towels. Treated sites were scored for erythema and edema at 0.5-1, 24, 48, 72 hours, and 7 and 14 days after removal of the patch. Individual results and irritation grades were presented.

The author noted that at various observation times there was a limited ability to score erythema due to dark discoloration of the test site resulting from the residue of the test article.

The test article was heated once to 80°C and again to approximately 40°C and stirred continuously using a motor driven propeller prior to being dispensed into an amber glass container .

RESULTS:

There was a wide range of reactions to the treatment (Attachment 1). One rabbit (45993 F) had no edema at any time and a very slight erythema (score = 1) which was observed only at the 0.5-1 hour period after treatment. Another rabbit (45992 F) still had well defined erythema (score = 2) on day 14 of observation and moderate edema (score = 3) on day 7 of observation. The remaining 4 rabbits had an intermediate degree of skin irritation (with scores no worse than very slight erythema or slight edema), all signs subsiding after 72 hours.

Signed and dated quality assurance and GLP compliance statements were present.

REVIEWER'S COMMENTS/DISCUSSION:

Calculation of the Primary Skin Irritation Score using the 24 and 72-hour values, as done by the Registrant, gave a value of 1.84. When the Primary Skin Irritation Score was calculated using the 0.5-1, 24, 48, and 72-hour values, as done by the Reviewer, its value was 1.54. Both values (<2) are consistent with a slight degree of irritation.

Based solely on the Primary Skin Irritation Score, the test material could go in Toxicity Category IV (mild or slight irritation at 72 hours). However, based (1) on the prolonged irritation, extending beyond the last observation day, seen in rabbit 45992 F (grade 3 edema on day 7 and grade 2 erythema on day 14) and (2) a potential for underestimation of irritation due to discoloration of the sites, a conservative estimation of the irritation potential of the test material places it in Toxicity Category III.

Attachment 1
From pp. 14-15 of the Study Report

IRDC

Individual Rabbit Scores and Score Calculation

TABLE 1.
Test Article
0.5 ml/test site

Individual Test Site Scores

Animal No.	Observation Time	ERYTHEMA Site # and Skin Treatment 1I	EDEMA Site # and Skin Treatment 1I
45991 M	HOUR 0.5-1	0	0
	HOUR 24	1	1
	HOUR 48	1	2
	HOUR 72	1	2
	DAY 7	0	0
45994 M	HOUR 0.5-1	0	0
	HOUR 24	1	1
	HOUR 48	1	1
	HOUR 72	1	1
	DAY 7	0	0
45989 F	HOUR 0.5-1	0	0
	HOUR 24	1	1
	HOUR 48	1	1
	HOUR 72	1	1
	DAY 7	0	0

I = Intact

671-009

Individual Rabbit Scores and Score Calculation

TABLE 1 CONT.
Test Article
0.5 ml/test site

Individual Test Site Scores

Animal No.	Observation Time	ERYTHEMA Site # and Skin Treatment 1I	EDEMA Site # and Skin Treatment 1I
45990 F	HOUR 0.5-1	1	0
	HOUR 24	1	0
	HOUR 48	0	0
	HOUR 72	0	0
45992 F	HOUR 0.5-1	1	0
	HOUR 24	1	2
	HOUR 48	2	3
	HOUR 72	2	3
	DAY 7	1	3
	DAY 14	2	0
45993 F	HOUR 0.5-1	1	0
	HOUR 24	0	0
	HOUR 48	0	0
	HOUR 72	0	0

Calculation for Primary Skin Irritation Score (Score = The average of the erythema scores plus the average of the edema scores at 24 and 72 hours after dosing): (10 ÷ 12) + (12 ÷ 12) = 1.8

I = Intact

671-009

Reviewed by: Alberto Protzel, Ph.D. Alberto Protzel 5/20/94
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D. James N. Rowe 5/23/94
Section III, Tox. Branch II(7509C)

DATA EVALUATION REPORT

STUDY TYPE: Dermal sensitization in guinea pigs;
EPA Guideline 81-6

EPA IDENTIFICATION: EPA MRID No. 430321-06
PC Code: 025004
DP Barcode: D197959
Submission: S453838

TEST MATERIAL: North American P1/P13 Creosote CTM

SYNONYMS: North American Creosote Composite P1/P13

STUDY NUMBER: 671-011

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Dermal Sensitization Study (Buehler) in the Albino Guinea Pig.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 22, 1993

EXECUTIVE SUMMARY: In a dermal sensitization study (the Buehler test), Crl:(HA) BR (Albino Hartley) VAF/Plus Guinea pigs (10 animals/sex) from Charles River Laboratories, Inc., Portage, MI, were induced dermally with North American P1/P13 Creosote CTM (100% in corn oil) on study days 1, 7 and 14. Three weeks after the final induction, the test animals were challenged dermally with North American P1/P13 Creosote CTM (3% in corn oil). The challenge reaction was somewhat stronger, but not clearly different from that observed in previously untreated controls. Upon rechallenge 1 week later (with 3% test material in corn oil), the test animals gave a stronger reaction than that seen in the initial challenge. The untreated controls, however, had an unexpectedly strong irritation reaction that made the testing results equivocal. Positive controls (induced and challenged with 2,4-DNCB) gave a response that was unexpectedly weak. This equivocal test must be repeated based on the unexpectedly high reaction of the untreated controls and the weak positive control reaction.

The study is classified as **Supplementary Data** and **does not satisfy** the requirement, § 81-6 for a dermal sensitization study in Guinea pigs (for North American P1/P13 Creosote CTM).

MATERIALS:

1. (a) Test compound: North American P1/P13 Creosote CTM. Description: Black liquid; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture derived from coal tar; its composition is detailed in MRID 424241-01. Additionally, Attachment 1 in the DER for MRID 430321-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P1/P13 in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. of the test material was stated to be 8001-58-9.

(b) Positive Control: 1-chloro-2,4-dinitrobenzene (2,4-DNCB). Lot. 69F 0232; from Sigma Chemical Co.

(c) Vehicles: Corn oil; Lot No. 1572.02; from Bio-Serv (French Town, NJ). Acetone; from EM Science (Gibbstown, NJ).

2. Test animals: Species: Guinea Pig; Strain: Crl:(HA) BR (Albino Hartley) VAF/Plus; Age: Approx. 1.5 to 3 months old; Weight (main study, at dosing): 418-910 g (males) and 410-743 g (females); Weight (screening study, at dosing): 390-818 g (males) and 353-612 g (females). Source: Charles River Laboratories, Inc., Portage, Michigan. Acclimation: 20-63 days.

METHODS:

Sensitization studies were conducted using Buehler's Method.

1. Irritation Screening:

An initial irritation screening study ("induction screen") was conducted to determine the concentration of test article to be used in the induction phase. A second irritation screening study ("challenge screen") was conducted between the induction and challenge phases to determine the concentration of test material to be used in the challenge phase.

Two or three application sites were shaved the day prior to test material administration. For the pre-induction screen the test material was administered as 75 or 100% mixtures in corn oil to 2 males and 1 female. For the pre-challenge screen, 0.1, 0.25, 0.50, 1, 3, 5, 10, 15, 25, 50, or 75% mixtures of test material in corn oil were applied to the animals grouped as shown in Table 2 using 20 x 20 mm Webril pads. The patches were occluded with medium gauge rubber dental dam. After the 6-hour exposure period, the patches were removed and the test sites wiped with a damp, disposable cloth. The test sites were scored for irritation approximately 24 and 48 hours after exposure.

2. Induction of Sensitization:

Forty guinea pigs were assigned to the study groups shown below in Table 1. The left shoulder of each guinea pig was clipped free of hair on the day prior to dosing. Test Material was administered as a 100% mixture in corn oil (0.4 ml) on a 20x20 mm Webril pad and then occluded with medium gauge rubber dental dam.

The patches were removed after a 6-hour exposure, and the sites were wiped with damp disposable toweling. A second and third induction were performed on the same test site on study days 7 and 14. **Positive control** animals were treated in a similar manner with 0.4 ml of 0.1% 2,4-DNCB in acetone for induction. **Untreated controls** remained untreated during the induction phase.

Table 1. Study groups for dermal sensitization studies with North American Creosote Composite P1/P13.

Group No.	Applied Material	Number of Animals	
		Male	Female
1	Untreated Control[a]	5	5
2	Positive Control (2,4-DNCB)	5	5
3	Test Material	10	10

[a] Noninduced; treated with test material during challenge phase only. An additional group of untreated controls (2M/5F) was used for re-challenge with test material. This latter group of controls was, apparently, not part of the forty guinea pigs initially assigned to study groups in this study. Its relation to the initial untreated controls is unclear.

3. Challenge Phase:
All guinea pigs, including the untreated controls were challenged on day 37, three weeks after the final induction. The left flank of each guinea pig was clipped free of hair on the day prior to dosing. Test animals and untreated controls were challenged with 0.4 ml of the test material as a 3% mixture in corn oil applied in the same manner as it was done for induction. Positive controls were challenged with 0.05% 2,4-DNCB in acetone. After the 6-hour exposures, the patches were removed and the test sites were wiped with damp disposable toweling. The test sites and the immediate surrounding area were depilated using NEET® lotion at approximately 20 hours after patch removal. The test sites were evaluated for irritation 2 hours after depilation ("24 hour observation") and again 24 hours later ("48 hour observation").

4. Re-challenge:
One week after challenge, the test group and a second group of untreated controls (Table 1) were re-challenged. New application sites were clipped and prepared on the right side of each animal. The patch sites were graded as was done in the challenge phase.

Signed and dated quality assurance and GLP compliance statements were present.

RESULTS:

1. Irritation screening:

The induction screen showed slight to moderate erythema (scores of 1-2) at 24 & 48 hours with the 100% concentration treatment. Therefore, the 100% concentration was used as the induction concentration.

Table 2. Individual erythema scores from the irritation screening study with North American P1/P13 Creosote CTM (Data from pp. 26-29 of the Study Report).

Conc. Level[a] (%)	Time[b] (Hrs)	Animal Number (sex)											
		12209 (M)	12210 (F)	12111 (F)	12201 (M)	12202 (M)	12203 (F)	12198 (M)	12199 (M)	12200 (F)	12195 (M)	12196 (M)	12197 (F)
0.10	24	±	±	±									
"	48	±	0	±									
0.25	24	1	±	1									
"	48	1	0	1									
0.50	24	1	1	±									
"	48	1	±	±									
1	24				1	nd[c]	±						
"	48				±	nd	±						
3	24				±	nd	1						
"	48				±	nd	1						
5	24				1	nd	2						
"	48				1	nd	1						
10	24							1	±	±			
"	48							1	±	±			
15	24							±	1	±			
"	48							±	1	±			
25	24										2	2	1
"	48										1	1	1
50	24										1	2	2
"	48										±	1	1
75	24										1	3	3
"	48										1	2	3

[a] Concentration of test material in corn oil.
[b] Time of observation for skin irritation.
[c] No data.

The challenge screen (Table 2) showed some degree of irritation at all concentrations used (0.1-75%) both at the 24- and 48-hour readings. Higher values (up to 2 and 3) were found at 25-75%, and lower values (down to 0 and ±) at 0.10%. Values of ± and 1 were found at 3%, the concentration that was selected for the challenge phase.

2. Challenge and Rechallenge Scores:

Results from the challenge with test material (3% in corn oil) appear in Table 3. Both controls and treated material had a similar reaction [30% incidence (irritation score ≥ 1) and mean irritation score of 0.6) at 24 hours. The incidence at 48 hours was clearly greater in test animals (60%) than in controls (10%); with some treated animals achieving scores of up to 2 and showing some edema.

Results from the rechallenge (done 1 week after challenge) with test material (3% in corn oil) appear in Table 4. The previously-challenged test animals showed an increase in incidence (to 80%) with increased severity (up to 3). Unexpectedly, the untreated controls (a different set of untreated controls) showed high incidence (100%) with high intensity (up to 3) scores after exposure to 3% test material. The intensity of this reaction is higher than that observed at higher concentrations in the preliminary screens (e.g. Table 2).

Results from the positive controls (2,4-DNCB) are shown in Attachment 1. Although a positive response was observed, the response was relatively weaker than expected.

REVIEWER'S COMMENTS/DISCUSSION:

Review of the irritation scores in Tables 3 and 4, indicates that the results of the test are equivocal, making this study inadequate to assess the dermal sensitization potential of North American P1/P13 Creosote CTM and should be repeated for the reasons discussed below.

Although the irritation scores of the induced animals rechallenged with test material increased in a fashion consistent with sensitization, evaluation of the results was confounded by the unexpectedly high irritation response of the rechallenge controls (Table 4). The intensity of the reaction of the rechallenge controls is higher and inconsistent with that observed even at higher concentrations in the preliminary screens (e.g. Table 2).

Although day-1 weights were given for the initial set of 40 guinea pigs, only weights "prior to testing" (day unspecified) were given for the rechallenge controls.

It is not clear if the unexpectedly high response of the rechallenge controls is related to their not being part of the initial group of 40 guinea pigs apportioned to study groups or if it reflects experimental problems (e.g. inadequate dispersion of test material).

Furthermore, the positive controls should have responded more severely and completely if the positive controls were adequately sensitized and/or challenged.

Table 3. Individual erythema scores following challenge with test material (North American P1/P13 Creosote CTM). Data from pp. 19 and 21 of the Study Report.

Untreated controls				Test material (3% in corn oil)			
Animal number	Sex	Erythema score		Animal number	Sex	Erythema score	
		24 hrs.	48 hrs.			24 hrs.	48 hrs.
12079	M	±	±	12099	M	±	1e[a]
12080	M	1	±	12100	M	±	2
12081	M	±	±	12101	M	0	0
12082	M	1	1	12102	M	1	1e
12083	M	±	±	12103	M	±	±
				12104	M	±	±
				12105	M	±	±
				12106	M	±	1
				12107	M	1	1
				12108	M	±	
12084	F	±	±	12109	F	±	0
12085	F	1	±	12110	F	±	±
12086	F	±	±	12111	F	1	1
12087	F	0	0	12112	F	1	1
12088	F	±	±	12113	F	±	1
				12114	F	1	1e
				12115	F	1	2e
				12116	F	±	±
				12117	F	±	±
				12118	F	±	1
Incidence (No. with score ≥ 1):		3/10	1/10	Incidence (No. with score ≥ 1)		6/20	12/20
Incidence index		0.3	0.1	Incidence index		0.3	0.6
Severity index (mean score)[b]		0.6	0.5	Severity index (mean score)		0.63	0.85

[a] e = edema also observed.

[b] In a scale of 0 to 4. The symbol " ± " corresponds to a score of 0.5.

Table 4. Individual erythema scores following re-challenge with test material (North American P1/P13 Creosote CTM). Data from pp. 19 and 21 of the Study Report.

Untreated controls[a]				Test material (3% in corn oil)			
Animal number	Sex	Erythema score		Animal number	Sex	Erythema score	
		24 hrs.	48 hrs.			24 hrs.	48 hrs.
12255	M	1	±	12099	M	1	±
12256	M	2	±	12100	M	2	1
				12101	M	2	1
				12102	M	1	1
				12103	M	±	±
				12104	M	2	1
				12105	M	1	1
				12106	M	2	1
				12107	M	3	2
				12108	M	±	±
12257	F	1	1	12109	F	1	1
12258	F	3	2	12110	F	2	1
12259	F	2	1	12111	F	±	1
12260	F	1	1	12112	F	±	±
12281	F	1	1	12113	F	1	1
				12114	F	2	±
				12115	F	2	1
				12116	F	2	2
				12117	F	3	2
				12118	F	2	1
Incidence (No. with score ≥ 1):		7/7	5/7	Incidence (No. with score ≥ 1)		16/20	15/20
Incidence index		1.0	0.7	Incidence index		0.8	0.8
Severity index (mean score)[b]		1.6	1.0	Severity index (mean score)		1.5	1.03

[a] A different set of controls than the one used in the Table 3 (challenge).
[b] In a scale of 0 to 4. The symbol " ± " corresponds to a score of 0.5.

Attachment 1
Individual Irritation Scores for Positive Controls
From p. 20 of the Study Report

Individual Erythema Scores Following Challenge

Group, Animal Number	Sex	Concentration Level 0.05% 24 Hour	48 Hour
2,4-DNCB:			
12089	M	±	±
12090	M	0	±
12091	M	1	2e
12092	M	0	±
12093	M	±	±
12094	F	±	1
12095	F	0	±
12096	F	1	2e
12097	F	±	2e
12098	F	±	2e
Incidence (number of animals exhibiting a score ≥ 1/number of animals tested:		2/10	5/10
Incidence index		0.2	0.5
Severity index:		0.45	1.15

671-011

e - edema also observed

Reviewed by: Alberto Protzel, Ph.D.
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D.
Section III, Tox. Branch II(7509C)

5/26/94

James N. Rowe 5/26/94

DATA EVALUATION REPORT

STUDY TYPE: Acute oral toxicity in rats;
EPA Guideline 81-1

EPA IDENTIFICATION : EPA MRID No. 430323-01
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P2 Creosote CTM

SYNONYMS: North American Creosote Composite P2 CTM

STUDY NUMBER: 671-002

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Acute Oral Toxicity Study in Rats.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 10, 1993

EXECUTIVE SUMMARY: In an acute oral toxicity study, Crl:CD^R BR VAF/Plus^R rats (5 rats/sex/dose) from Charles River Laboratories, Inc., Portage, MI were administered orally North American P2 Creosote CTM suspended in corn oil at doses of 1000, 1500, 2000, 2300, 3000, or 3500 mg/kg/b.w. The acute oral LD_{50} values for males and females were 2524 and 1993 mg/kg, respectively. Pharmacotoxic signs observed during the 13 days following dosing included material around the mouth/nose and prostration.

The study is classified as Core Minimum Data (Acceptable) with a Toxicity Category III (LD_{50} from >500 through 5000 mg/kg) and satisfies the requirement, § 81-1 for an acute oral toxicity study in rats (for North American P2 Creosote CTM).

MATERIALS:

1. Test compound: North American P2 Creosote CTM. Description: Black liquid; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424237-01. Additionally, Attachment 1 in the DER for MRID 430323-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P2 CTM in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. was stated as 65996-92-1.

2. Test animals: Species: rat, Strain: Charles River Crl:CD^{R} BR VAF/Plus^{R}, albino, Sprague-Dawley; Age: 8-10 weeks old; Weight (at dosing): 229-313 g (males) and 161-199 g (females); Source: Charles River Laboratories, Inc., Portage, MI; acclimatization: 11-23 days.

METHODS:

Rats were fasted for about 18-20 hours before dosing. Test material was administered orally by gavage to 5 rats/sex/dose in corn oil in a volume of 10 ml/kg to give doses of 1000, 1500, 2000, 2300, 3000, or 3500 mg/kg/b.w. Animals were observed for mortality at 1, 2, and 4 hours after dosing on the first day and twice daily for 13 additional days. Pharmacotoxic signs were monitored at 1, 2, and 4 hours after dosing and once daily for 13 additional days. Rats were weighed prior to dosing, on day 8 and at study termination (day 15) or when the animal was found dead. All animals were necropsied for gross pathological examination.

The author noted that the test article was heated once to 80°C and again to approximately 40°C and stirred continuously using a motor driven propeller prior to being dispensed into an amber glass container. As noted in Attachment 2 in the DER for MRID 430323-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P2 CTM in Rats), the primary container with test material received from the sponsor (a 55-gallon drum) was heated to 80°C with a drum heater and stirred for 72 hours in order to obtain a homogeneous mixture. The test material was then transferred from the primary container to 32 secondary, 1-gallon containers for use in various tests. Prior to each test run, the secondary container was heated to 40°C and stirred.

RESULTS:

Pharmacotoxic signs during the first 4 hours after dosing included decreased activity at all dose levels (90-100%), low carriage (40-100%) at all levels except at 3000 mg/kg, where the incidence was 20% Decreased limb tone was seen in 50% of the rats at 3500 mg/kg. Material around the nose was seen in all rats with 90-100% incidence at 3000 and 3500 mg/kg. Pharmacotoxic signs observed during the 13 days following dosing included material around the mouth/nose (50-90%) at $\geq$ 2000 mg/kg, prostration (60-90%) and was observed at levels $\geq$ 2000 mg/kg. Mortality data are summarized in Table 1. The LD_{50} values for males and females were 2524 and 1993 mg/kg, respectively.

Gross necropsy revealed a distended urinary bladder (20% at 3000 mg/kg and 30% at 3500 mg/kg),and red foci in the glandular stomach 40%, 50%, and 30% at 2000, 3000 and 3500 mg/kg, respectively. Two females had inhibited body weight gain at 2000 mg/kg on day 15; no other effects on body weight gain were observed.

No effects on weight gain were observed.

Table 1. Mortality in rats after a single oral dose of North American P2 Creosote CTM (From p. 11 of the Study Report).

Dose mg/kg	Males deaths/dosed	Females deaths/dosed
1000	0/5	0/5
1500	0/5	0/5
2000	1/5	3/5
2300	2/5	4/5
3000	3/5	5/5
4000	5/5	5/5
LD_{50}(95%CL)[a]	2524(2178-2926) mg/kg	1993(1781-2230) mg/kg

[a] The combined LD_{50}(95%CL) for males and females was 2236 (2014-2482) mg/kg.

Signed and dated quality assurance and GLP compliance statements were present.

Reviewed by: Alberto Protzel, Ph.D.
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D.
Section III, Tox. Branch II(7509C)

Alberto Protzel 5/23/94
James N. Rowe 5/23/94

DATA EVALUATION REPORT

STUDY TYPE: Acute dermal toxicity in rabbits;
EPA Guideline 81-2

EPA IDENTIFICATION: EPA MRID No. 430323-02
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P2 Creosote CTM

SYNONYMS: North American Creosote Composite P2

STUDY NUMBER: 671-004

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Acute Dermal Toxicity Study in Rabbits.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 9, 1993

EXECUTIVE SUMMARY: In an acute dermal toxicity study, New Zealand White (Hra:(NZW)SPF) rabbits (5 rabbits/sex/dose) from Hazleton Research Products, Inc., Kalamazoo, MI were administered undiluted North American Creosote Composite P2, 2000 mg/kg b.w., to a shaved area in the back of approximately 15% of the body surface for 24 hours. No deaths or abnormal clinical signs were observed in any dose group. The acute dermal LD_{50} is greater than 2000 mg/kg for both sexes.

The study is classified as **Core Minimum Data** (Acceptable) with a **Toxicity Category III** and satisfies the requirement, § 81-2 for an acute dermal toxicity study in rabbits (for North American P2 Creosote CTM).

MATERIALS:

1. Test compound: North American P2 Creosote CTM. Description: Black liquid; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424237-01. Additionally, Attachment 1 in the DER for MRID 430323-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P2 CTM in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. was stated as 65996-92-1.

2. Test animals: Species: rabbit, Strain: New Zealand White (Hra:(NZW)SPF); Age: Approx. 3 1/2 months old; Weight (at dosing): 2410-2531 g (males) and 2260-2491 g (females); Source: Hazleton Research Products, Inc., Kalamazoo, Michigan. Quarantine: 18 days.

METHODS:

Groups of five male and five female rabbits had 2000 mg/kg of test material applied evenly (as received with no dilution) to a shaved area of the back. Hair was removed on the day prior to dosing with an electric clipper. The application area comprised approximately 15% of the body surface of the rabbit (1.83 ml/kg). The test area was covered with gauze and secured with Dermiform^{R} tape. Twenty four hours after treatment, the dressing was removed and the treated site was washed with water and dried with disposable towels. The rabbits were observed for mortality 1, 2, and 4 hours after dosing on the first day, and twice daily for 13 additional days. The rabbits were observed for pharmacotoxic signs at 1, 2, and 4 hours after dosing on the first day, and once daily for 13 additional days. Body weights were determined prior to dosing, on day 8 and at study termination (day 15). Necropsy was performed on all animals.

The test article was heated once to 80°C and again to approximately 40°C and stirred continuously using a motor driven propeller prior to being dispensed into an amber glass container.

RESULTS:

No animals died during the study. No pharmacotoxic signs or body weight effects were seen and no abnormalities were observed at gross necropsy that appeared to be treatment-related.

Signed and dated quality assurance and GLP compliance statements were present.

Based on the above information it is concluded that the dermal LD_{50} was > 2000 mg/kg.

Reviewed by: Alberto Protzel, Ph.D.
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D.
Section III, Tox. Branch II(7509C)

Alberto Protzel 4/12/94
James N. Rowe 4/18/94

DATA EVALUATION REPORT

STUDY TYPE: Acute inhalation toxicity in rats; EPA Guideline 81-3

EPA IDENTIFICATION: EPA MRID No. 430323-03
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P2 Creosote CTM

SYNONYMS: North American Creosote Composite P2 CTM

STUDY NUMBER: 671-006

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Acute Inhalation Toxicity Evaluation on North American Creosote Composite P2 CTM in Rats.

AUTHOR(S): Roger J. Hilaski

REPORT ISSUED: November 10, 1993

EXECUTIVE SUMMARY: In an acute inhalation toxicity study, Sprague-Dawley derived Crl:CD^{R} BR VAF/Plus^{R} rats (5 rats/sex/dose level) from Charles River Laboratories, Inc., Portage, MI; were exposed to North American P2 Creosote CTM as an aerosol at nominal levels of 10.9 and 9.9 mg/l, corresponding to respective mean analytical levels of 5.3 (MMAD = 2.9 μm) and 0.6 (MMAD = 1.3 μm) mg/l. There was no mortality among treated rats. All low-dose and high-dose rats exhibited decreased activity immediately after exposure. At the high dose, all males and 4/5 females exhibited decreased activity during the 14-day observation period. **The 4-hour inhalation LC_{50} for North American P2 Creosote CTM is greater than 5.3 mg/l in rats.**

This study is classified as Core Minimum with TOXICITY CATEGORY of IV for INHALATION (4-hr LC_{50} > 5 mg/l). This study **satisfies** the requirement, § 81-3 for an acute inhalation toxicity (LC_{50}) study in rats.

MATERIALS:

1. Test compound: North American P2 Creosote CTM. Description: Black liquid; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424237-01. Additionally, a list of the components in the test material having concentrations greater than 0.5% appears in Attachment 1 of this DER. The CAS No. of the test material was stated to be 65996-92-1.

2. Test animals: Species: rat; Strain: Sprague-Dawley derived Crl:CD^{R} BR VAF/Plus^{R}; Age: at least 54 days of age; Weight (at dosing): 248-279 g (males) and 172-224 g (females); Source: Charles River Laboratories, Inc., Portage, MI; acclimatization: at least 12 days.

METHODS:

Groups of five male and five female rats per dose were exposed (whole body exposure) for 4 hours to North American P2 Creosote CTM as an aerosol, at nominal levels of 10.9 and 9.9 mg/l, corresponding to respective mean analytical levels of 5.3 (Group I) and 0.6 (Group II) mg/l.

The animals were observed for mortality and toxic signs following exposure. The animals were observed for toxic signs (once daily) and for mortality (twice daily) during the 14-day post-exposure period. Body weights were recorded before exposure, and at 7 and 14 days post-exposure. All animals were subjected to gross pathological observation. No tissues were saved.

It was noted by the authors (Attachment 2 of this DER) that, initially, the primary container with test material received from the sponsor (a 55-gallon drum) was heated to 80°C with a drum heater and stirred for 24 hours in order to obtain a homogeneous mixture. The test material was then transferred from the primary container to 33 secondary, 1-gallon containers for use in various tests. Prior to each test run, the secondary container containing the test material aliquot used in the study was heated to 40°C and stirred.

To generate the exposure atmospheres, the test material was pumped to a Spraying Systems atomizer for formation of an aerosol that was discharged into a 4-liter glass atomization chamber. Purge-airflow swept the aerosol from the atomization chamber into the 160-liter stainless steel and glass exposure chamber. The exposure chamber was exhausted into a fume hood. Chamber airflow rates were 36 l/min (about 13.5 chamber volumes/hour at the high dose) and 106 l/min (about 39.7 chamber volumes/hour at the low dose). The exposure atmosphere was sampled (4 samples/dose; site and time of sampling were unspecified) at rates of 1-2 liters/minute for total volumes of 6 liters. Test material was collected in tared glass fiber filters for determination of chamber concentrations. Aerosol particle size distribution was determined with an Andersen^{R} 8-stage cascade impactor.

Although the author indicated that the animals were housed in individual steel wire cages it was not explicitly indicated that the animals were in individual cages during exposure.

RESULTS:

The analytical concentrations (in mg/l) were:
low dose (Group II): Mean of 0.6 and standard deviation of 0.05.
high dose (Group I): Mean of 5.3 and standard deviation of 0.32

The mass median aerodynamic diameter (MMAD) was:
- 2.9 μm (geometric standard deviation of 1.86) at 5.3 mg/l, and
- 1.3 μm (geometric standard deviation of 1.80) at 0.6 mg/l.

There were no deaths in this study and no significant macroscopic abnormalities were noted at necropsy. The following effects were observed:

- Low dose (0.6 mg/l, Group II): All animals exhibited decreased activity immediately after exposure. Additionally, 4 males and 4 females had increased salivation and 1 male and 4 females had increased lacrimation immediately after exposure. No significant pharmacotoxic signs were observed during the 14-day post-exposure period. Body weight gain was depressed for males on week 1 and for females for weeks 1 and 2 after exposure.

- High dose (5 mg/l, Group I): Immediately after exposure all animals were stained with the black test material, exhibited decreased activity, and 1 male and 1 female had excessive lacrimation. All males and 3/5 females exhibited decreased activity during the 14-day observation period. Body weight gain was depressed for males on week 1 and for females for weeks 1 and 2 after exposure.

The LC_{50} for North American Creosote Composite P2 is greater than 5.3 mg/l for a 4-hour exposure.

Signed and dated quality assurance and GLP compliance statements were present.

Attachment 1
From page 38 of the Study Report.

Table 1. Creosote Target Analytes Greater than 0.5% by weight in P1 and P2 Composite Test Mixture Creosotes.

Target Analytes	P1 Composite (%)	P2 Composite (%)
Dihydroindene (Indan)	0.67 ± .004	0.67 ± .014
Indene	1.45 ± .010	1.22 ± .027
Naphthalene	10.86 ± .079	10.99 ± .249
Benzo(b)thiophene	0.48 ± .011	0.51 ± .009
Quinoline	1.30 ± .012	1.47 ± .044
2-Methylnaphthalene	5.37 ± .035	5.23 ± .189
1-Methylnaphthalene	2.68 ± .020	2.64 ± .070
Biphenyl	1.21 ± .011	1.31 ±.053
Acenaphthene	6.27 ± .045	7.00 ±.271
Dibenzofuran	4.80 ± .039	5.74 ± .222
Fluorene	4.27 ± .030	4.94 ± .188
Dibenzothiophene	1.44 ± .083	1.53 ± .121
Phenanthrene	12.66 ± .681	13.51 ± .901
Anthracene	1.33 ± .074	1.42 ± .097
Carbazole	1.23 ± 0.56	1.23 ± .076
4H-cyclopenta[*de*]phenanthrene	1.84 ± .038	1.80 ± .151
Fluorenthene	6.90 ± .299	6.92 ± .451
Pyrene	5.47 ± .234	5.34 ± .348
2,3-Benzofluorene	1.04 ± .033	1.01 ± .082
Benz(a)anthracene	1.02 ± .055	1.00 ± .082
Chrysene	0.99 ± .007	1.04 ± .079
Benzo(b)fluoranthene	0.58 ± .014	0.57± .054
Benzo(k)fluoranthene**	0.23 ± .006	0.23 ± .027
Total % (by weight)	74.09 ± 1.58	77.32 ± 3.30

**Benzo(k)fluoranthene was determined to be greater than the 0.5% by weight using GC/MS so it was included in this list.

Attachment 2
From page 7 of the Study Report .

As a Percent (%) of Creosote	Date Analyzed 8/26/92	8/31/92	Reported Composition(%)*
Naphthalene	8.50	8.55	10.99
2-Methylnaphthalene	5.05	4.29	5.23
1-Methylnaphthalene	1.76	1.82	2.64
Acenaphthene	5.53	5.64	7.00
Dibenzofuran	3.53	3.71	5.74
Fluoranthene	4.16	4.14	4.94
Phenanthrene	12.2	12.7	13.51
Fluoranthene	5.86	5.92	6.92
Pyrene	4.54	4.34	5.34

*Quantitative and qualitative determination of Creosote by Gas Chromatography/Flame Ionization (GC/FID), Geochemical and Environmental Research Group (GERG), SOP-9206, July 23, 1992.

When development studies began, the primary container (55-gallon drum) was heated to 80°C with a drum heater and stirred for 72 hours prior to use in order to obtain a homogenous mixture. The test material was transferred from the primary container to 32 secondary containers (approximately one gallon each). Prior to all test runs and exposures, the secondary container was heated to 40°C and stirred. The test material and compound reservoir were examined for any undissolved/unsuspended solids, if a sediment was observed, the material was allowed to mix while heating for additional time (1.5 hours) until it was sediment free. If no sediment was found, then the material was used. The test material was heated and stirred throughout the test runs and exposures.

METHODS

EXPERIMENTAL DESIGN:

The study was designed to determine the acute inhalation toxicological effects in rats exposed, whole-body, to North American P2 Creosote CTM.

The experimental design was conducted such that the first exposure level was at a concentration of 5 mg/L or the maximum obtainable concentration at any respirable aerosol size. Since no deaths occurred, the second exposure level was performed at the maximum obtainable concentration where at least 25% of the aerosol was one micrometer (or less) in diameter.

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Reviewed by: Alberto Protzel, Ph.D. 4/12/94
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D. 4/18/94
Section III, Tox. Branch II(7509C)

DATA EVALUATION REPORT

STUDY TYPE: Primary Eye Irritation in rabbits;
EPA Guideline 81-4

EPA IDENTIFICATION: EPA MRID No. 430323-04
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P2 Creosote CTM

SYNONYMS: North American Creosote Composite P2

STUDY NUMBER: 671-008

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Eye Irritation Study in Rabbits.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 9, 1993

EXECUTIVE SUMMARY: In a primary eye irritation study, New Zealand White (Hra:(NZW)SPF) rabbits (3 males and 3 females) from Hazleton Research Products, Inc., Kalamazoo, MI were administered 0.1 ml of undiluted North American Creosote Composite P2 into the cupped conjunctival sac of the right eye. The cornea, iris and conjunctiva were scored (Draize) for eye irritation. There was no corneal or iridial irritation. Irritation of the conjunctiva (in 3/6 animals) was seen at 96 hours of observation but not on day 7 of observation.

The study is classified as **Core Minimum Data** (Acceptable) with a **Toxicity Category III** and **satisfies** the requirement, § 81-4 for a primary eye irritation study in rabbits (for North American P2 Creosote CTM).

MATERIALS:

1. Test compound: North American P2 Creosote CTM. Description: Black liquid with pH of 9; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424237-01. Additionally, Attachment 1 in the DER for MRID 430323-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P2 CTM in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. was stated as 65996-92-1.

2. Test animals: Species: rabbit, Strain: New Zealand White (Hra:(NZW)SPF); Age: Approx. 3 1/2 months old; Weight (at dosing): 2558-2898 g (males) and 2429-2522 g (females); Source: Hazleton Research Products, Inc., Kalamazoo, Michigan. Quarantine: 16 days.

METHODS:

One group of 3 male and 3 female rabbits was administered 0.1 ml of test material/rabbit into the cupped conjunctival sac of the right eye. The eyelids were gently held together for one second after administration. The eyes remained unwashed. The left eye was manipulated as the right eye, but received no test material and served as control. The rabbits were observed for the occurrence of vocalization. Both eyes were examined according to a Draize scale at 1, 24, 48, 72, and 96 hours and at 7 days after dosing. Sodium fluorescein examinations were conducted at 72 hours and at 7 days. The animals were observed for mortality once during the day of treatment and twice daily during the subsequent observation period. Individual data for each rabbit were presented.

The test article was heated once to 80°C and again to approximately 40°C and stirred continuously using a motor driven propeller prior to being dispensed into an amber glass container .

RESULTS:

No animals died and no overt signs of toxicity were observed during the study. No vocalization or signs of distress were observed. No effects were observed on the cornea or the iris of the six rabbits (all corneal and iris scores were 0). Fluorescein staining was negative. There was conjunctival redness (maximum scores of 2) in all animals for 24-96 hours. Three of six animals had conjunctival redness through 96 hours, achieving a score of 0 at day 7 of observation. Chemosis was observed in all rabbits for at least 1 hour. One of six animals showed chemosis (score of 2: obvious swelling with partial eversion of lids) through 96 hours, achieving a score of 0 at day 7 of observation. Three of six animals had some degree of discharge, limited to the first day after exposure. Average eye irritation scores at 96 hours and day 7 were 4.0 and 0.0, respectively.

The test material is classified as belonging in Toxicity Category III (irritation clearing in 7 days or less). It is noted that another creosote blend (North American P1/P13 Creosote CTM) has a primary eye irritation toxicity category of

II in rabbits (Study No. 671-007; EPA MRID No. 430321-06).

Signed and dated quality assurance and GLP compliance statements were present.

Reviewed by: Alberto Protzel, Ph.D.
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D.
Section III, Tox. Branch II(7509C)

Alberto Protzel 5/25/94
James N. Rowe 5/25/94

DATA EVALUATION REPORT

STUDY TYPE: Primary Dermal Irritation in rabbits;
EPA Guideline 81-5

EPA IDENTIFICATION: EPA MRID No. 430323-05
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P2 Creosote CTM

SYNONYMS: North American Creosote Composite P2

STUDY NUMBER: 671-010

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Primary Dermal Irritation Test in Rabbits.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 9, 1993

EXECUTIVE SUMMARY: In a primary skin irritation study, a 1 in^2 area of intact skin of New Zealand White rabbits (3 males and 3 females) from Hazleton Research Products, Inc., Kalamazoo, MI, was exposed to 0.5 ml of undiluted North American Creosote Composite P2 for 4 hours. At 72 hours, two rabbits had edema scores of 2, the others had scores of 0 or 1. No irritation (all scores were 0) was observed after 72 hours.

The study is classified as **Core Supplementary Data** with an assignment to a toxicity category deferred, pending submission of additional information. This study does **not satisfy** the requirement, § 81-5 for a primary skin irritation study in rabbits. This study may be **upgraded to Core Minimum** if the following additional information is provided and is judged to be acceptable:

1. Rationale for euthanization of two rabbits at 72 hours while the rest were euthanized at 7 days.
2. A clarification concerning the "two groups" that were terminated due to technician error: Were these groups already treated with test material? Had they been scored for dermal irritation? If so, what were their irritation scores?

MATERIALS:

1. Test compound: North American P2 Creosote CTM. Description: Black liquid with pH of 5; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture; its composition is detailed in MRID 424237-01. Additionally, Attachment 1 in the DER for MRID 430323-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P2 CTM in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. was stated as 65996-92-1.

2. Test animals: Species: rabbit; Strain: New Zealand White; Age: Approx. 3 1/2 months old; Weight (at dosing): 2416-2527 g (males) and 2298-2453 g (females); Source: Hazleton Research Products, Inc., Kalamazoo, Michigan. Acclimation: 9 days.

METHODS:

The dorsal hair of six rabbits (3 males, 3 females) was clipped using electric clippers. One application (intact skin) site on the back was delineated with indelible marker. A total of 0.5 ml of the test material was applied undiluted to the site (approximately 1 in^2). The site was covered with 1 in^2 gauze patch, secured with strips of non-irritating tape and then wrapped with 8-ply gauze bandaging and Dermiform® tape. Four hours after treatment, dressings were removed and the test area was washed thoroughly with water and dried with disposable towels. Treated sites were scored for erythema and edema at 0.5-1, 24, 48, 72 hours and (if applicable) 7 and 14 days after removal of the patch. Two rabbits were euthanized after 72 hours of observation, no rationale was offered. Individual results and irritation grades were presented.

The author noted that at various observation times there was a limited ability to score erythema due to dark discoloration of the test site resulting from the residue of the test article.

The test article was heated once to 80°C and again to approximately 40°C and stirred continuously using a motor driven propeller prior to being dispensed into an amber glass container .

RESULTS:

Erythema was observed in 3/6 rabbits, starting at 24-hours and lasting through the 72-hour observation period (with a maximum score of 2 for one of the rabbits, Attachment 1). Edema was observed in 5/6 rabbits, starting at 24 hours and not extending beyond the 72-hour observation period. At 72 hours, two rabbits had edema scores of 2, the others had scores of 0 or 1. No irritation (all scores were 0) was observed after 72 hours.

Two rabbits (46000 M and 45999 F) lacked observations after 72 hours; presumably these rabbits were the ones that were euthanized, but the author did not indicate so.

Signed and dated quality assurance and GLP compliance statements were present.

REVIEWER'S COMMENTS/DISCUSSION:

Although the author indicated that two rabbits (presumably 46000 M and 45999 F) were euthanized after the 72-hour observation the authors did not give a rationale for doing so. Additionally, the author indicated that "two groups were terminated due to technician error" and no additional data were given.

This study is classified as Supplementary, but may be upgraded to Minimum, if the following additional information is provided and is judged to be acceptable:

1. Rationale for euthanization of two rabbits at 72 hours while the rest were euthanized at 7 days.

2. A clarification concerning the "two groups" that were terminated due to technician error: Were these groups already treated with test material? Had they been scored for dermal irritation? If so, what were their irritation scores?

Attachment 1
From pp. 14-15 of the Study Report

IRDC

Individual Rabbit Scores and Score Calculation

TABLE 1.
Test Article
0.5 ml/test site

Individual Test Site Scores

Animal No.	Observation Time	ERYTHEMA Site # and Skin Treatment 1I	EDEMA Site # and Skin Treatment 1I
45997 M	HOUR 0.5-1	0	0
	HOUR 24	1	2
	HOUR 48	1	2
	HOUR 72	1	2
	DAY 7	0	0
45998 M	HOUR 0.5-1	0	0
	HOUR 24	1	2
	HOUR 48	2	2
	HOUR 72	2	2
	DAY 7	0	0
46000 M	HOUR 0.5-1	0	0
	HOUR 24	0	1
	HOUR 48	0	0
	HOUR 72	0	0

I = Intact

671-010

Individual Rabbit Scores and Score Calculation

TABLE 1 CONT.
Test Article
0.5 ml/test site

Individual Test Site Scores

Animal No.	Observation Time	ERYTHEMA Site # and Skin Treatment 1I	EDEMA Site # and Skin Treatment 1I
45995 F	HOUR 0.5-1	0	0
	HOUR 24	0	0
	HOUR 48	0	1
	HOUR 72	0	1
	DAY 7	0	0
45996 F	HOUR 0.5-1	0	0
	HOUR 24	0	1
	HOUR 48	1	1
	HOUR 72	1	1
	DAY 7	0	0
45999 F	HOUR 0.5-1	0	0
	HOUR 24	0	0
	HOUR 48	0	0
	HOUR 72	0	0

Calculation for Primary Skin Irritation Score (Score = The average of the erythema scores plus the average of the edema scores at 24 and 72 hours after dosing): (6 ÷ 12) + (12 ÷ 12) = 1.5

I = Intact

671-010

Reviewed by: Alberto Protzel, Ph.D.
Section III, Tox. Branch II(7509C)
Secondary reviewer: James N. Rowe, Ph.D.
Section III, Tox. Branch II(7509C)

Alberto Protzel 5/20/94
James N. Rowe 5/23/94

DATA EVALUATION REPORT

STUDY TYPE: Dermal sensitization in guinea pigs; EPA Guideline 81-6

EPA IDENTIFICATION: EPA MRID No. 430323-06
PC Code: 025004
DP Barcode: D197959
Submission: S455838

TEST MATERIAL: North American P2 Creosote CTM

SYNONYMS: North American Creosote Composite P2

STUDY NUMBER: 671-012

SPONSOR: Creosote Council II and Trenton Sales, Inc of Houston, TX.

TESTING FACILITY: International Research and Development Corporation, Mattawan MI.

TITLE OF REPORT: Dermal Sensitization Study (Buehler) in the Albino Guinea Pig.

AUTHOR(S): J.A. Wisler

REPORT ISSUED: November 22, 1993

EXECUTIVE SUMMARY: In a dermal sensitization study (the Buehler test), Crl:(HA) BR (Albino Hartley) VAF/Plus Guinea pigs (10 animals/sex) from Charles River Laboratories, Inc., Portage, MI, were induced dermally with North American P2 Creosote CTM (75% in corn oil) on study days 1, 7 and 14. Two weeks after the final induction, the test animals were challenged dermally with North American P2 Creosote CTM (3% in corn oil). The challenge reaction was more severe in the test animals than in controls, but the incidence was not clearly different in test animals (100%) than in controls (70%). The untreated controls had an unexpectedly high and variable reaction which made the evaluation of the results of this test equivocal. This equivocal test must be repeated based on the unexpectedly high and variable reaction of the untreated controls

The study is classified as Supplementary Data and does not satisfy the requirement, § 81-6 for a dermal sensitization study in Guinea pigs (for North American P2 Creosote CTM).

MATERIALS:

1. (a) Test compound: North American P2 Creosote CTM. Description: Black liquid; Lot. No.: Not applicable; Purity: The test material is a standard blend produced by the sponsor from creosotes from various industry sources. This material is a complex, multicomponent mixture derived from coal tar; its composition is detailed in MRID 424237-01. Additionally, Attachment 1 in the DER for MRID 430323-03 (Acute Inhalation Toxicity Evaluation on North American Creosote Composite P2 CTM in Rats) contains a list of the components in the test material having concentrations greater than 0.5%. The CAS No. was stated as 65996-92-1.
(b) Positive Control: 1-chloro-2,4-dinitrobenzene (2,4-DNCB). Lot. 69F 0232; from Sigma Chemical Co.
(c) Vehicles: Corn oil; Lot No. 1572.02; from Bio-Serv (French Town, NJ). Acetone; from EM Science (Gibbstown, NJ).

2. Test animals: Species: Guinea Pig; Strain: Crl:(HA) BR (Albino Hartley) VAF/Plus; Age: Approx. 3 months old; Weight (main study, at dosing): 355-428 g (males) and 340-390 g (females); Weight (screening study, at dosing): 380-582 g (males) and 366-585 g (females). Source: Charles River Laboratories, Inc., Portage, Michigan. Acclimation: 15 days.

METHODS:

Sensitization studies were conducted using Buehler's Method.

1. Irritation Screening:

An irritation screening study (pre-induction screen) was conducted to determine the concentration of test article to be used in the induction phase. A second irritation screening study (pre-challenge screen) was conducted between the induction and challenge phases to determine the concentration of test material to be used in the challenge phase

Two or three application sites were shaved the day prior to test material administration. The test material was administered to 3 animals (2M & 1F) as 50, 75 or 100% mixtures in corn oil at the pre-induction screen and as a 3% mixture in corn oil to 3 animals (2M & 1F) at the pre-challenge screen using 20 x 20 mm Webril pads. The patches were occluded with medium gauge rubber dental dam. After the 6-hour exposure period, the patches were removed and the test sites wiped with a damp, disposable cloth. The test sites were scored for irritation approximately 24 and 48 hours after exposure. Skin irritation was assessed according to the following scale:

0	: no reaction;
± (0.5)	: slight, patchy erythema;
1	: slight confluent or moderate, but patchy erythema;
2	: moderate confluent erythema;
3	: severe erythema, with or without edema.

2. Induction of Sensitization:

Forty guinea pigs were assigned to the study groups shown below in Table 1. The left shoulder of each guinea pig was clipped free of hair on the day prior to dosing. **Test Material** was administered as a 75% mixture in corn oil (0.4 ml) on a 20x20 mm Webril pad and then occluded with medium gauge rubber dental dam. The patches were removed after a 6-hour exposure, and the sites were wiped with damp disposable toweling. A second and third induction were performed on the same test site on study days 7 and 14. **Positive control** animals were treated in a similar manner with 0.4 ml of 0.1% 2,4-DNCB in acetone for induction. **Untreated controls** remained untreated during the induction phase.

Table 1. Study groups for dermal sensitization studies with North American Creosote Composite P2.

Group No.	Applied Material	Number of Animals	
		Male	Female
1	Untreated Control[a]	5	5
2	Positive Control (2,4-DNCB)	5	5
3	Test Material	10	10

[a] Noninduced; treated with test material during challenge phase only.

3. Challenge Phase:

All guinea pigs, including the untreated controls were challenged on day 29, two weeks after the final induction. The left flank of each guinea pig was clipped free of hair on the day prior to dosing. Test animals and untreated controls were challenged with 0.4 ml of the test material as a 3% mixture in corn oil applied in the same manner as it was done for induction. Positive controls were challenged with 0.05% 2,4-DNCB in acetone. After the 6-hour exposures, the patches were removed and the test sites were wiped with damp disposable toweling. The test sites and the immediate surrounding area were depilated using NEET® lotion at approximately 18 hours after patch removal. The test sites were evaluated for irritation 2 hours after depilation ("24 hour observation") and again 24 hours later ("48 hour observation").

4. Re-challenge:
There was no rechallenge.

Signed and dated quality assurance and GLP compliance statements were present.

RESULTS:

1. Irritation screening:

The screening results of the pre-induction and pre-challenge screens appear in Table 2. The results of the pre-induction irritation screen showed a slight

irritation at 50% with some increase at 100%. Even though the pre-challenge screen was done with 3% test material, the irritation scores were unexpectedly higher that those observed at the 50% and 75% levels in the pre-induction screen.

2. Challenge Scores:

Results from the challenge with test material (3% in corn oil) appear in Table 3. At 24 hours, the severity was clearly higher in the test animals (2.15) than in the controls (1.05). The incidence (irritation score $\geq$ 1) in the controls (70%), although smaller that in the test animals (100%) was still higher than that observed with the 50% and 75% concentrations in the irritation screen of Table 2. The reaction at 48 hours in the test animals remained clearly higher in incidence and in severity than that observed for the controls.

The positive controls (Attachment 1) achieved incidences of 100% and 90% at 24 and 48 hours, respectively.

Table 2. Individual erythema scores from the pre-induction and pre-challenge screens with North American P2 Creosote CTM (From pages 21 and 22 of the Study Report).

Testing Phase	Animal Number	Sex	Concentration Level							
			3%		50%		75%		100%	
			24 Hr.	48 Hr.	24 Hr.	48 Hr.	24 Hr.	48 Hr.	24 Hr.	48 Hr.
Pre-Induction Screen										
	12152	M			±	±	0	0	±	±
	12153	M			±	1	1	1	2	2
	12154	F			0	±	±	±	1	1
Pre-Challenge Screen										
	12252	M	2[a] / 1	1 / 1						
	12253	M	2 / 2	2 / 2						
	12254	F	2 / 2	2 / 1						

[a] The slash (/) separates readings from two sites on the same animal.

Table 3. Individual erythema scores following challenge with test material (North American P2 Creosote CTM). Data from pp. 17 and 19 of the Study Report.

Untreated controls				Test material (3% in corn oil)			
Animal number	Sex	Erythema score		Animal number	Sex	Erythema score	
		24 hrs.	48 hrs.			24 hrs.	48 hrs.
12155	M	1	0	12175	M	1	1
12156	M	2	1	12176	M	2	2
12157	M	1	±	12177	M	2	1
12158	M	1	±	12178	M	3e[a]	2e
12159	M	±	±	12179	M	2	1
				12180	M	3e	3e
				12181	M	2	±
				12182	M	2	2e
				12183	M	1	±
				12184	M	1	±
12160	F	1	±	12185	F	1	1
12161	F	1	±	12186	F	3e	3e
12162	F	±	0	12187	F	2	±
12163	F	2	±	12188	F	3e	2e
12164	F	±	±	12189	F	2	1
				12190	F	3e	2e
				12191	F	3e	3e
				12192	F	2	2e
				12193	F	2	1
				12194	F	3e	3e
Incidence (No. with score ≥ 1):		7/10	1/10	Incidence (No. with score ≥ 1)		20/20	16/20
Incidence index		0.7	0.1	Incidence index		1.0	0.8
Severity index (mean score)[b]		1.05	0.4	Severity index (mean score)		2.15	1.6

[a] e = edema also observed.

[b] In a scale of 0 to 4. The symbol " ± " corresponds to a score of 0.5.

REVIEWER'S COMMENTS/DISCUSSION:

Review of the irritation scores in Tables 2 and 3, indicates that the results of the test are equivocal, making this study inadequate to assess the dermal sensitization potential of North American P2 Creosote CTM and should be repeated for the reasons discussed below.

Although the irritation scores of the induced animals challenged with test material were suggestive of a potential for sensitization, evaluation of the results was confounded by the unexplained variability of the response of the controls. The reaction of the controls at 24 hours, although less intense than in the 3% screen, was more intense and inconsistent with that observed at the 50% and 75% levels used in the pre-induction screen.

Attachment 1
Individual Irritation Scores for Positive Controls
From p. 18 of the Study Report

IRDC

Individual Erythema Scores Following Challenge

Animal Number	Sex	Concentration Level 0.5% 24 Hour	48 Hour
Positive Control:			
12165	M	3 e	3 e
12166	M	2 e	2 e
12167	M	1	±
12168	M	3 e	3 e
12169	M	2 e	3 e
12170	F	3 e	3 e
12171	F	2 e	2
12172	F	3 e	3 e
12173	F	3 e	2 e
12174	F	2 e	3 e
Incidence (number of animals exhibiting) a score ≥ 1/number of animals tested		10/10	9/10
Incidence Index:		1.0	0.9
Severity Index:		2.4	2.45

e - edema

13544

009139

Chemical:	**Coal tar creosote**
PC Code:	**025004**
HED File Code	**13000 Tox Reviews**
Memo Date:	***06/07/1994***
File ID:	**TX011033**
Accession Number:	***412-01-0083***

HED Records Reference Center
01/11/2001